グリオキサルのラット及びマウスを用いた
経口投与によるがん原性予備試験(混水試験)報告書

試験番号

2 週間試験：ラット/0222；マウス/0223

APPENDIX

APPENDIXES

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIX A 1-1

CLINICAL OBSERVATION (TWO-WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-1 1	1-2 1	1-3 1	1-4 1	1-5 1	1-6 1	1-7 1	2-1 1	2-2 1	2-3 1	2-4 1	2-5 1	2-6 1	2-7 1
DEATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9000ppm	0	0	0	0	0	0	0	0	0	1	1	1	1	1
MORIBUND SACRIFICE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9000ppm	0	0	0	0	0	0	0	0	0	1	4	4	4	4
LOCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9000ppm	0	0	0	0	0	0	0	0	0	3	3	0	0	0
HUNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9000ppm	0	0	0	0	0	0	0	0	2	5	5	2	2	3
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	1	1	1	1	1
	9000ppm	0	0	0	0	0	0	0	7	7	7	6	4	4	5

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-1 1	1-2 1	1-3 1	1-4 1	1-5 1	1-6 1	1-7 1	2-1 1	2-2 1	2-3 1	2-4 1	2-5 1	2-6 1	2-7 1
IRREGULAR BREATHING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9000ppm	0	0	0	0	0	0	0	0	0	1	2	1	1	1
ABNORMAL RESPIRATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9000ppm	0	0	0	0	0	0	0	0	0	1	2	1	1	1
SMALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	1	1	1	1	1	1	1	0
	9000ppm	0	0	0	0	9	9	9	9	9	8	7	4	4	4
OLIGO-STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	1	1	1	1	0
	9000ppm	0	0	0	0	4	4	4	4	4	8	7	5	5	4
SUBNORMAL TEMP	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9000ppm	0	0	0	0	0	0	0	0	0	1	3	1	1	1

APPENDIX A 1-2

CLINICAL OBSERVATION (TWO-WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 1-1 1	1-2 1	1-3 1	1-4 1	1-5 1	1-6 1	1-7 1	2-1 1	2-2 1	2-3 1	2-4 1	2-5 1	2-6 1	2-7 1
DEATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	0	1	1
	9000ppm	0	0	0	0	0	0	0	1	2	2	2	2	4	5
MORIBUND SACRIFICE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9000ppm	0	0	0	0	0	0	1	1	2	2	4	4	4	4
LOCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	1	0	0
	9000ppm	0	0	0	0	0	0	1	0	1	0	0	1	1	0
HUNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	1	1	2	2	1	1
	9000ppm	0	0	0	0	0	2	3	1	5	6	6	4	2	1
SOILED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9000ppm	0	0	0	0	0	0	0	0	1	1	1	0	1	0

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 1-1 1	1-2 1	1-3 1	1-4 1	1-5 1	1-6 1	1-7 1	2-1 1	2-2 1	2-3 1	2-4 1	2-5 1	2-6 1	2-7 1
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	1	2	3	3	3	2	3
	9000ppm	0	0	0	0	0	2	2	6	7	6	6	4	2	1
SOILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	1	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	1	1	2	2	2	4	4	4	2	5
	9000ppm	0	0	0	0	3	3	6	5	4	5	6	4	2	1
IRREGULAR BREATHING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	1	0	0
	9000ppm	0	0	0	0	0	0	1	0	1	1	3	2	1	0
ABNORMAL RESPIRATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	1	0	0
	9000ppm	0	0	0	0	0	0	1	0	1	1	3	2	1	0
SMALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	3	3	3	2	2	2	2	1
	9000ppm	0	0	0	0	7	7	10	8	7	6	6	4	2	1

Clinical sign	Group Name	Administration Week-day 1-1 1	1-2 1	1-3 1	1-4 1	1-5 1	1-6 1	1-7 1	2-1 1	2-2 1	2-3 1	2-4 1	2-5 1	2-6 1	2-7 1
OLIGO-STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	1	1	1	1	2	2	2	2	1	1
	9000ppm	0	0	0	0	3	3	5	3	4	6	6	4	2	1
SUBNORMAL TEMP	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	1	0	0
	9000ppm	0	0	0	0	0	0	1	0	1	0	2	1	0	0

APPENDIX A 1-3

CLINICAL OBSERVATION (TWO-WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-1	1-2	1-3	1-4	1-5	1-6	1-7	2-1	2-2	2-3	2-4	2-5	2-6	2-7
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9000ppm	0	0	0	0	0	0	0	0	0	1	1	1	1	1
SMALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	1
OLIGO-STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9000ppm	0	0	0	0	1	1	1	1	1	1	1	1	1	1

APPENDIX A 1-4

CLINICAL OBSERVATION (TWO-WEEK STUDY: SUMMARY)

MOSUE: FEMALE

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 1-1	1-2	1-3	1-4	1-5	1-6	1-7	2-1	2-2	2-3	2-4	2-5	2-6	2-7
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
SMALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9000ppm	0	0	0	0	1	1	0	0	0	0	0	0	0	0
OLIGO-STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9000ppm	0	0	0	0	1	1	0	0	0	0	0	0	0	0

APPENDIX A 2-1

BODY WEIGHT CHANGES (TWO-WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0222
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-1	1-2	1-4	1-7	2-3	2-7
Control	128± 5	133± 5	136± 5	143± 5	154± 7	166± 8	178± 10
1778ppm	128± 5	128± 4	132± 4	139± 3	149± 3	160± 4	170± 5
2667ppm	128± 4	126± 4**	128± 5**	134± 5**	144± 6	155± 7	165± 8*
4000ppm	128± 5	124± 5**	121± 5**	121± 7**	129± 9**	139± 10**	149± 11**
6000ppm	128± 5	121± 5**	116± 5**	110± 7**	109± 11**	113± 15**	122± 14**
9000ppm	128± 5	119± 5**	111± 4**	100± 5**	87± 9**	79± 12**	85± 13**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 2-2

BODY WEIGHT CHANGES (TWO-WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0222
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-1	1-2	1-4	1-7	2-3	2-7
Control	106± 4	109± 4	110± 5	112± 5	119± 5	124± 5	129± 6
1778ppm	106± 4	105± 4	107± 4	111± 4	117± 4	122± 5	126± 5
2667ppm	106± 4	103± 4*	104± 5*	108± 5	112± 6	118± 7	122± 8
4000ppm	106± 4	101± 4**	98± 4**	100± 5**	106± 6**	111± 6*	116± 6**
6000ppm	106± 4	99± 4**	94± 4**	89± 6**	89± 9**	91± 14**	103± 10**
9000ppm	106± 4	93± 4**	91± 4**	82± 3**	70± 5**	64± 2**	68± 0 ?

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX A 2-3

BODY WEIGHT CHANGES (TWO-WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-1	1-2	1-4	1-7	2-3	2-7
Control	23.6± 0.8	23.1± 1.0	23.4± 1.0	23.9± 1.2	24.0± 1.2	24.0± 1.2	24.5± 1.2
1778ppm	23.6± 0.9	23.1± 0.8	23.4± 0.7	24.0± 0.6	24.4± 0.6	24.4± 0.7	24.7± 0.8
2667ppm	23.6± 0.9	22.7± 1.0	22.9± 1.2	23.6± 1.1	24.0± 1.2	23.7± 1.2	24.1± 1.4
4000ppm	23.6± 0.9	22.3± 0.9	22.4± 1.0	23.2± 1.2	23.6± 1.1	23.7± 1.4	24.0± 1.1
6000ppm	23.6± 0.9	21.6± 0.7**	21.6± 0.6**	22.4± 0.6**	22.8± 0.8	23.2± 0.8	23.3± 0.8
9000ppm	23.6± 0.8	21.3± 0.7**	20.7± 0.7**	20.9± 1.2**	21.4± 2.0**	21.7± 2.4**	21.7± 2.7**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 2-4

BODY WEIGHT CHANGES (TWO-WEEK STUDY: SUMMARY)

MOSUE: FEMALE

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-1	1-2	1-4	1-7	2-3	2-7
Control	18.9± 0.6	18.6± 0.5	18.4± 0.3	19.0± 0.5	19.1± 0.3	19.4± 0.5	19.8± 0.5
1778ppm	18.9± 0.8	18.2± 0.7	18.5± 0.6	18.7± 0.7	19.1± 0.8	19.3± 1.1	19.6± 0.8
2667ppm	18.9± 0.8	17.7± 0.7*	17.8± 0.8	18.4± 0.8	18.9± 0.7	18.8± 0.8	19.2± 0.9
4000ppm	18.9± 0.6	17.6± 0.7**	17.6± 0.8*	18.6± 0.8	18.9± 0.8	19.0± 0.9	19.4± 0.9
6000ppm	18.9± 0.8	16.9± 0.8**	16.6± 0.6**	17.5± 0.7**	18.3± 0.8*	18.8± 0.6	18.9± 0.6*
9000ppm	18.9± 0.6	16.6± 0.6**	15.8± 0.4**	16.2± 0.6**	17.1± 0.7**	17.9± 0.8**	18.3± 0.6**

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 3-1

WATER CONSUMPTION CHANGES : SUMMARY, RAT: MALE

(TWO-WEEK STUDY)

STUDY NO. : 0222
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-3(3)	1-7(4)	2-3(3)	2-7(4)
Control	16.5± 1.7	16.7± 2.9	17.8± 3.6	16.6± 3.6
1778ppm	11.8± 0.8	11.4± 0.6	12.7± 0.8	10.6± 0.6
2667ppm	10.2± 1.2	10.8± 1.0*	12.5± 1.5*	10.0± 1.1**
4000ppm	7.4± 1.2**	10.0± 0.4**	11.6± 0.7**	9.2± 0.4**
6000ppm	4.6± 0.6**	6.6± 2.2**	9.9± 2.5**	9.2± 1.3**
9000ppm	2.8± 0.4**	2.8± 0.5**	4.9± 1.6**	4.6± 0.0 ?

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX A 3-2

WATER CONSUMPTION CHANGES : SUMMARY, RAT: FEMALE

(TWO-WEEK STUDY)

STUDY NO. : 0222
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-3(3)	1-7(4)	2-3(3)	2-7(4)
Control	17.8± 1.0	17.9± 1.3	19.4± 1.6	18.7± 1.4
1778ppm	13.1± 0.7**	13.5± 0.9**	15.2± 1.1**	13.6± 0.8**
2667ppm	11.4± 0.5**	13.5± 1.0**	14.3± 1.1**	12.9± 1.0**
4000ppm	7.7± 1.2**	11.1± 2.0**	13.8± 1.5**	12.3± 1.8**
6000ppm	4.6± 0.7**	6.3± 1.7**	9.1± 2.1**	9.0± 0.9**
9000ppm	3.1± 0.6**	3.1± 1.3**	3.7± 1.5**	4.8± 1.2**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 3-3

WATER CONSUMPTION CHANGES : SUMMARY, MOUSE: MALE

(TWO-WEEK STUDY)

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-3(3)	1-7(4)	2-3(3)	2-7(4)
Control	3.9± 0.3	4.0± 0.4	3.9± 0.2	3.9± 0.4
1778ppm	3.2± 0.2	3.2± 0.2	3.1± 0.4	3.0± 0.5
2667ppm	2.6± 0.3*	2.8± 0.2*	2.5± 0.2*	2.5± 0.4*
4000ppm	2.1± 0.3**	2.4± 0.3**	2.1± 0.3**	2.0± 0.3**
6000ppm	1.5± 0.2**	2.1± 0.2**	1.8± 0.1**	1.7± 0.2**
9000ppm	1.0± 0.1**	1.7± 0.4**	1.5± 0.3**	1.5± 0.2**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX 3-4

WATER CONSUMPTION CHANGES : SUMMARY, MOUSE: FEMALE

(TWO-WEEK STUDY)

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-3(3)	1-7(4)	2-3(3)	2-7(4)
Control	4.3± 0.3	4.5± 0.3	4.5± 0.4	4.5± 0.3
1778ppm	3.1± 0.4	3.1± 0.4**	3.2± 0.3**	3.2± 0.4
2667ppm	2.6± 0.2	2.8± 0.2**	2.8± 0.2**	2.7± 0.2
4000ppm	2.1± 0.1**	2.7± 0.2**	2.4± 0.2**	2.4± 0.2**
6000ppm	1.4± 0.1**	2.2± 0.2**	2.1± 0.2**	1.7± 0.1**
9000ppm	0.9± 0.1**	1.8± 0.2**	1.8± 0.2**	1.8± 0.3**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 4-1

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(TWO-WEEK STUDY)

STUDY NO. : 0222
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)
Control	13.8± 1.1	14.9± 1.2
1778ppm	12.5± 0.5*	13.8± 0.6
2667ppm	11.8± 0.6**	13.6± 0.8*
4000ppm	9.3± 1.3**	12.3± 1.2**
6000ppm	6.7± 1.0**	9.4± 1.5**
9000ppm	4.3± 0.9**	5.7± 1.2**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 4-2

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(TWO-WEEK STUDY)

STUDY NO. : 0222
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)
Control	11.0± 0.8	11.2± 1.0
1778ppm	10.2± 0.5	11.0± 0.7
2667ppm	9.2± 0.7	10.6± 1.1
4000ppm	7.7± 0.7**	10.0± 0.7*
6000ppm	5.1± 1.0**	8.5± 1.3**
9000ppm	3.3± 0.3**	5.0± 0.0 ?

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX A 4-3

FOOD CONSUMPTION CHANGES : SUMMARY, MOSUE : MALE

(TWO-WEEK STUDY)

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration 1-7(7)	week-day(effective) 2-7(7)
Control	3.5± 0.3	3.6± 0.3
1778ppm	3.5± 0.2	3.6± 0.2
2667ppm	3.4± 0.3	3.5± 0.2
4000ppm	3.2± 0.2	3.5± 0.3
6000ppm	3.1± 0.2**	3.5± 0.2
9000ppm	2.9± 0.1**	3.5± 0.6

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 4-4

FOOD CONSUMPTION CHANGES : SUMMARY, MOSUE : FEMALE

(TWO-WEEK STUDY)

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)
Control	3.2± 0.1	3.5± 0.2
1778ppm	3.0± 0.3	3.3± 0.2
2667ppm	2.8± 0.2**	3.2± 0.2**
4000ppm	2.7± 0.2**	3.1± 0.2**
6000ppm	2.6± 0.1**	3.1± 0.2**
9000ppm	2.3± 0.2**	3.1± 0.2**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 5-1

CHEMICAL INTAKE CHANGES: SUMMARY, RAT : MALE

(TWO-WEEK STUDY)

STUDY NO. : 0222
ANIMAL : RAT F344
UNIT : mg/kg/d a y
REPORT TYPE : A1 2
SEX : MALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2
Control	0.000± 0.000	0.000± 0.000
1778ppm	161.190± 10.745	141.687± 7.012
2667ppm	248.546± 14.154	209.708± 10.901
4000ppm	344.458± 40.708	330.614± 27.033
6000ppm	343.547± 68.453	443.380± 56.195
9000ppm	312.579± 93.832	503.930± 98.662

APPENDIX A 5-2

CHEMICAL INTAKE CHANGES: SUMMARY, RAT : FEMALE

(TWO-WEEK STUDY)

STUDY NO. : 0222
ANIMAL : RAT F344
UNIT : mg／kg／d a y
REPORT TYPE : A1 2
SEX : FEMALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2
Control	0.000± 0.000	0.000± 0.000
1778ppm	173.780± 6.369	148.622± 6.046
2667ppm	257.772± 17.610	217.256± 12.508
4000ppm	379.251± 15.156	318.364± 13.830
6000ppm	434.232±112.501	539.051± 64.246
9000ppm	357.556± 63.374	608.823± 0.000

APPENDIX A 5-3

CHEMICAL INTAKE CHANGES: SUMMARY, MOUSE: MALE

(TWO-WEEK STUDY)

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
UNIT : mg/kg/day
REPORT TYPE : A1 2
SEX : MALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2
Control	0.000± 0.000	0.000± 0.000
1778ppm	234.124± 14.368	216.479± 34.901
2667ppm	307.359± 17.599	276.649± 40.298
4000ppm	400.214± 40.871	335.646± 44.561
6000ppm	554.876± 33.224	443.647± 36.612
9000ppm	706.584±114.095	613.979± 80.015

APPENDIX A 5-4

CHEMICAL INTAKE CHANGES: SUMMARY, MOUSE: FEMALE

(TWO-WEEK STUDY)

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
UNIT : mg/kg/d a y
REPORT TYPE : A1 2
SEX : FEMALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2
Control	0.000± 0.000	0.000± 0.000
1778ppm	287.564± 30.333	285.549± 38.652
2667ppm	398.985± 18.132	379.188± 22.742
4000ppm	566.778± 45.094	495.016± 43.414
6000ppm	710.398± 56.520	552.528± 35.704
9000ppm	946.025± 70.351	858.567±134.228

APPENDIX A 6-1

HEMATOLOGY (TWO-WEEK STUDY : SUMMARY)

RAT : MALE

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$		HEMOGLOBIN g/dℓ		HEMATOCRIT %		MCV fℓ		MCH pg		MCHC g/dℓ		PLATELET $10^3/\mu\ell$	
Control	5	8.00±	0.25	15.1±	0.6	44.6±	1.2	55.7±	0.5	18.8±	0.3	33.8±	0.8	922±	35
1778ppm	5	7.97±	0.09	15.2±	0.1	44.0±	0.8	55.3±	0.4	19.0±	0.3	34.4±	0.7	909±	37
2667ppm	5	8.13±	0.24	15.5±	0.4	45.3±	1.0	55.7±	0.5	19.1±	0.3	34.3±	0.4	907±	47
4000ppm	5	8.15±	0.23	15.4±	0.3	44.9±	1.2	55.1±	0.5	18.9±	0.3	34.4±	0.5	837±	14
6000ppm	5	8.51±	0.17	16.4±	0.5*	47.2±	1.1	55.5±	0.6	19.2±	0.4	34.7±	0.4	650±	169*
9000ppm	5	9.68±	0.85**	18.7±	1.6**	54.8±	7.0**	56.5±	2.2	19.3±	0.1	34.3±	1.3	304±	162**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	RETICULOCYTE ‰	PROTHROMBIN TIME sec	APTT sec
Control	5	48± 6	12.7± 0.5	19.3± 2.3
1778ppm	5	41± 10	12.8± 0.3	19.4± 2.7
2667ppm	5	40± 13	12.7± 0.5	20.8± 2.0
4000ppm	5	38± 4	12.9± 0.8	21.2± 2.3
6000ppm	5	21± 12**	13.5± 0.3	20.3± 2.6
9000ppm	5	11± 7**	15.3± 0.0 ?	23.3± 0.0 ?

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	5	6.20± 1.47	0± 0	15± 4	1± 1	0± 0	3± 2	81± 4	0± 0
1778ppm	5	4.99± 0.65	0± 0	13± 2	1± 1	0± 0	2± 1	84± 2	0± 0
2667ppm	5	5.25± 0.97	0± 1	12± 4	1± 1	0± 0	3± 1	83± 4	0± 0
4000ppm	5	4.89± 1.26	0± 0	14± 2	1± 0	0± 0	4± 1	81± 2	0± 0
6000ppm	5	5.04± 1.62	0± 0	20± 5	1± 1	0± 0	4± 1	75± 6	0± 0
9000ppm	5	3.44± 0.71**	0± 0	29± 10	2± 2	0± 0	4± 1	66± 10	0± 0

Significant difference ; * : $P \leqq 0.05$ ** : $P \leqq 0.01$ Test of Dunnett

APPENDIX A 6-2

HEMATOLOGY (TWO-WEEK STUDY : SUMMARY)

RAT : FEMALE

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	5	8.29± 0.21	15.7± 0.4	46.0± 1.0	55.6± 0.3	19.0± 0.5	34.2± 0.9	919± 34
1778ppm	5	8.28± 0.11	16.2± 0.3	46.0± 0.7	55.5± 0.3	19.5± 0.3	35.2± 0.4	821± 66
2667ppm	5	8.44± 0.25	16.3± 0.6	46.5± 1.4	55.1± 0.4	19.4± 0.2	35.1± 0.3	758± 75*
4000ppm	5	8.21± 0.18	15.9± 0.5	45.1± 1.2	54.9± 0.4*	19.4± 0.5	35.3± 1.1	729± 101*
6000ppm	5	8.46± 0.18	16.1± 0.4	46.5± 0.8	55.0± 0.4	19.0± 0.5	34.6± 0.8	665± 140**
9000ppm	0	-	-	-	-	-	-	-

Significant difference ; * : $P \leqq 0.05$ ** : $P \leqq 0.01$ Test of Dunnett

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	RETICULOCYTE ‰	PROTHROMBIN TIME sec	APTT sec
Control	5	28± 7	13.2± 0.6	20.0± 2.7
1778ppm	5	27± 8	12.9± 0.2	18.5± 3.1
2667ppm	5	28± 4	13.3± 0.7	21.9± 5.1
4000ppm	5	32± 5	13.7± 0.8	21.2± 1.8
6000ppm	5	29± 10	13.9± 0.4	18.7± 1.9
9000ppm	0	-	-	-

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	5	4.43± 0.65	0± 0	15± 5	2± 1	0± 0	4± 1	80± 4	0± 0
1778ppm	5	4.17± 1.27	0± 1	15± 4	2± 1	0± 0	4± 2	79± 7	0± 1
2667ppm	5	5.25± 1.28	0± 0	12± 1	2± 1	0± 0	3± 1	84± 2	0± 0
4000ppm	5	5.01± 1.31	0± 0	15± 4	1± 1	0± 0	3± 1	81± 2	0± 0
6000ppm	5	4.20± 1.42	0± 0	28± 12	2± 1	0± 0	3± 1	67± 12	0± 0
9000ppm	0	-	-	-	-	-	-	-	-

Significant difference ; * : $P \leqq 0.05$ ** : $P \leqq 0.01$ Test of Dunnett

APPENDIX A 6-3

HEMATOLOGY (TWO-WEEK STUDY : SUMMARY)

MOUSE: MALE

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	5	10.53± 0.25	15.8± 0.3	47.6± 1.3	45.1± 0.3	15.0± 0.2	33.2± 0.5	1373± 122
1778ppm	5	10.36± 0.12	15.5± 0.2	46.9± 1.0	45.3± 0.6	15.0± 0.2	33.1± 0.5	1258± 99
2667ppm	5	10.69± 0.52	16.2± 0.6	48.4± 2.4	45.3± 0.7	15.1± 0.2	33.4± 0.5	1273± 114
4000ppm	5	10.57± 0.22	15.9± 0.2	47.8± 1.2	45.3± 0.7	15.0± 0.2	33.2± 0.5	1238± 28
6000ppm	5	10.73± 0.37	16.3± 0.4	47.9± 1.3	44.7± 0.9	15.2± 0.3	34.0± 0.1*	1214± 42
9000ppm	5	11.29± 0.45*	17.1± 0.7**	51.3± 2.5*	45.4± 1.0	15.2± 0.2	33.4± 0.4	1270± 91

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	5	2.23± 1.05	0± 0	14± 9	2± 2	0± 0	3± 1	82± 11	0± 0
1778ppm	5	2.07± 0.76	1± 0	11± 3	2± 1	0± 0	3± 1	84± 3	0± 0
2667ppm	5	3.01± 1.04	1± 1	12± 4	2± 1	0± 0	2± 1	83± 5	0± 0
4000ppm	5	2.21± 0.71	0± 1	12± 1	2± 2	0± 0	2± 2	84± 2	0± 0
6000ppm	5	1.97± 0.58	0± 0	10± 2	1± 1	0± 0	2± 2	86± 4	0± 0
9000ppm	5	1.87± 1.62	3± 7	19± 20	2± 1	0± 0	3± 1	73± 26	0± 0

Significant difference ; * : $P \leqq 0.05$ ** : $P \leqq 0.01$ Test of Dunnett

(HCL071)

APPENDIX A 6-4

HEMATOLOGY (TWO-WEEK STUDY : SUMMARY)

MOUSE: FEMALE

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	TOTAL PROTEIN g／dℓ	ALBUMIN g／dℓ	A/G RATIO	T-BILIRUBIN mg／dℓ	GLUCOSE mg／dℓ	T-CHOLESTEROL mg／dℓ	PHOSPHOLIPID mg／dℓ
Control	5	6.0± 0.1	3.6± 0.1	1.5± 0.1	0.35± 0.07	190± 11	61± 2	124± 5
1778ppm	5	5.9± 0.1	3.5± 0.1	1.5± 0.0	0.34± 0.08	190± 6	53± 2	105± 5
2667ppm	5	5.9± 0.1	3.5± 0.1	1.5± 0.0	0.33± 0.14	205± 17	52± 3	99± 7
4000ppm	5	5.9± 0.1	3.5± 0.1	1.5± 0.1	0.39± 0.06	193± 16	53± 3	97± 5*
6000ppm	5	5.7± 0.3	3.6± 0.2	1.6± 0.1*	0.51± 0.10	167± 33	57± 12	86± 10**
9000ppm	5	5.3± 0.3**	3.3± 0.2	1.7± 0.2*	0.39± 0.12	115± 39*	58± 18	73± 22**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	GOT IU/ℓ		GPT IU/ℓ		LDH IU/ℓ		G-GTP IU/ℓ		CPK IU/ℓ		UREA NITROGEN mg/dℓ		CREATININE mg/dℓ	
Control	5	57±	2	21±	2	221±	44	1±	0	168±	20	17.1±	1.1	0.4±	0.1
1778ppm	5	53±	4	11±	2*	164±	20	1±	0	125±	5	20.1±	3.2	0.4±	0.1
2667ppm	5	54±	3	10±	1**	203±	40	1±	0	174±	45	19.8±	2.7	0.4±	0.1
4000ppm	5	55±	3	10±	2**	199±	39	1±	0	177±	37	20.1±	2.7	0.4±	0.1
6000ppm	5	66±	14	11±	2*	243±	60	1±	0	195±	40	23.7±	6.7*	0.3±	0.1
9000ppm	5	123±	81	20±	12	242±	68	1±	1	185±	31	33.7±	16.9**	0.3±	0.0

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	SODIUM mEq／ℓ		POTASSIUM mEq／ℓ		CHLORIDE mEq／ℓ		CALCIUM mg／dℓ		INORGANIC PHOSPHORUS mg／dℓ	
Control	5	142±	1	4.2±	0.3	105±	1	10.9±	0.1	8.7±	0.8
1778ppm	5	141±	2	4.3±	0.3	107±	1	10.9±	0.2	6.8±	1.8
2667ppm	5	142±	1	3.9±	0.4	107±	1	10.9±	0.2	6.5±	1.2
4000ppm	5	142±	2	3.9±	0.6	107±	1	11.1±	0.6	6.3±	1.2
6000ppm	5	143±	2	3.6±	0.1	108±	2	11.2±	0.2	4.9±	1.0**
9000ppm	5	158±	17*	3.5±	0.3*	124±	19**	10.1±	0.5*	6.6±	2.1

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 7-1

BIOCHEMISTRY (TWO-WEEK STUDY : SUMMARY)

RAT : MALE

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	5	9.87± 0.66	15.3± 0.7	44.5± 2.2	45.1± 0.7	15.5± 0.4	34.3± 0.4	1003± 55
1778ppm	5	9.95± 0.26	15.2± 0.2	44.4± 0.8	44.6± 0.8	15.3± 0.3	34.3± 0.3	1080± 81
2667ppm	5	9.80± 0.45	15.1± 0.5	44.0± 1.8	44.9± 0.5	15.4± 0.3	34.4± 0.6	1047± 145
4000ppm	5	10.05± 0.23	15.2± 0.4	44.5± 0.8	44.3± 1.0	15.2± 0.4	34.2± 0.5	1138± 74
6000ppm	5	10.13± 0.43	15.8± 0.7	45.8± 2.1	45.2± 0.8	15.6± 0.1	34.5± 0.6	1052± 47
9000ppm	5	10.40± 0.38	16.0± 0.6	46.7± 1.8	44.9± 0.9	15.4± 0.2	34.2± 0.6	1027± 84

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

(HCL070)

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	5	1.78± 1.00	0± 1	10± 3	1± 1	0± 0	3± 1	86± 4	0± 0
1778ppm	5	1.93± 0.51	0± 0	11± 2	2± 1	0± 0	2± 1	85± 2	0± 0
2667ppm	5	2.06± 0.82	0± 0	8± 2	2± 1	0± 0	2± 1	88± 3	0± 0
4000ppm	5	2.29± 0.78	1± 1	12± 2	3± 2	0± 0	3± 1	82± 2	0± 0
6000ppm	5	1.95± 1.04	0± 1	11± 3	2± 2	0± 0	2± 1	84± 6	0± 0
9000ppm	5	2.98± 2.22	0± 0	11± 1	2± 1	0± 0	3± 2	84± 3	0± 0

Significant difference ; * : $P \leqq 0.05$ ** : $P \leqq 0.01$ Test of Dunnett

APPENDIX A 7-2

BIOCHEMISTRY (TWO-WEEK STUDY : SUMMARY)

RAT : FEMALE

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	TOTAL PROTEIN g/dℓ	ALBUMIN g/dℓ	A/G RATIO	T-BILIRUBIN mg/dℓ	GLUCOSE mg/dℓ	T-CHOLESTEROL mg/dℓ	PHOSPHOLIPID mg/dℓ
Control	5	5.8± 0.0	3.5± 0.1	1.5± 0.1	0.46± 0.13	196± 13	66± 2	120± 6
1778ppm	5	5.7± 0.1	3.5± 0.1	1.6± 0.0	0.49± 0.10	196± 18	57± 7	103± 14
2667ppm	5	5.7± 0.2	3.5± 0.1	1.6± 0.1	0.47± 0.08	188± 9	53± 7**	92± 12**
4000ppm	5	5.6± 0.1	3.5± 0.1	1.7± 0.1*	0.41± 0.08	192± 9	49± 3**	83± 7**
6000ppm	5	5.8± 0.2	3.6± 0.1	1.7± 0.1**	0.36± 0.06	155± 20**	51± 7**	78± 9**
9000ppm	0	-	-	-	-	-	-	-

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	GOT IU/ℓ	GPT IU/ℓ	LDH IU/ℓ	G-GTP IU/ℓ	CPK IU/ℓ	UREA NITROGEN mg/dℓ	CREATININE mg/dℓ
Control	5	61± 3	19± 2	231± 37	2± 0	151± 34	18.1± 3.0	0.4± 0.0
1778ppm	5	57± 5	10± 2**	255± 90	1± 1	133± 22	22.0± 2.1	0.4± 0.1
2667ppm	5	63± 2	10± 1**	254± 98	1± 1	143± 28	22.2± 2.9	0.3± 0.1
4000ppm	5	79± 40	20± 21	359± 389	2± 0	156± 29	22.4± 2.7	0.3± 0.0
6000ppm	5	70± 7*	12± 3	279± 77	1± 1	188± 36	22.8± 3.8	0.3± 0.0
9000ppm	0	-	-	-	-	-	-	-

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	5	142± 1	3.7± 0.4	107± 2	10.9± 0.7	7.4± 1.2
1778ppm	5	141± 1	3.6± 0.2	107± 1	10.5± 0.2	6.4± 1.4
2667ppm	5	142± 1	3.6± 0.1	108± 1	10.4± 0.1	5.9± 1.1
4000ppm	5	141± 1	3.8± 0.3	109± 1	10.4± 0.1	5.8± 1.2
6000ppm	5	142± 1	4.3± 0.3*	108± 1	11.1± 0.5	5.5± 0.6
9000ppm	0	-	-	-	-	-

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 7-3

BIOCHEMISTRY (TWO-WEEK STUDY : SUMMARY)

MOUSE: MALE

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	TOTAL PROTEIN g／dℓ	ALBUMIN g／dℓ	A/G RATIO	T-BILIRUBIN mg／dℓ	GLUCOSE mg／dℓ	T-CHOLESTEROL mg／dℓ	GOT I U／ℓ
Control	5	5.4± 0.4	3.0± 0.1	1.2± 0.2	0.29± 0.04	306± 33	97± 13	32± 1
1778ppm	5	5.2± 0.2	2.9± 0.1	1.3± 0.1	0.26± 0.08	317± 10	77± 4*	33± 4
2667ppm	5	5.4± 0.4	3.0± 0.2	1.2± 0.1	0.30± 0.11	286± 29	83± 18	34± 3
4000ppm	5	5.1± 0.1	2.8± 0.0	1.2± 0.1	0.30± 0.15	292± 22	77± 4*	33± 4
6000ppm	5	5.0± 0.2	2.8± 0.1	1.3± 0.1	0.25± 0.09	285± 20	75± 6*	33± 2
9000ppm	5	5.4± 0.5	3.1± 0.4	1.3± 0.1	0.34± 0.13	235± 59	80± 8	53± 34

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

(HCL074)

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	GPT IU/ℓ		LDH IU/ℓ		CPK IU/ℓ		UREA NITROGEN mg/dℓ		SODIUM mEq/ℓ		POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ	
Control	5	15±	1	208±	91	41±	15	25.1±	2.9	150±	3	4.8±	0.6	117±	3
1778ppm	5	12±	2	202±	49	60±	43	22.5±	1.7	150±	1	4.5±	0.5	119±	2
2667ppm	5	11±	2	213±	84	45±	15	26.4±	5.6	151±	1	4.7±	0.5	117±	1
4000ppm	5	13±	2	198±	55	45±	22	25.2±	4.8	150±	3	4.4±	0.4	116±	3
6000ppm	5	10±	2	187±	18	32±	5	28.0±	1.6	150±	2	4.2±	0.5	117±	1
9000ppm	5	14±	7	269±	91	85±	61	38.2±	16.0	162±	20	4.6±	0.6	123±	10

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	5	9.6± 0.9	7.6± 1.1
1778ppm	5	9.3± 0.2	8.0± 1.0
2667ppm	5	9.6± 0.5	8.6± 2.3
4000ppm	5	9.2± 0.2	8.0± 2.0
6000ppm	5	9.1± 0.2	7.4± 1.5
9000ppm	5	9.5± 0.5	7.3± 0.9

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 7-4

BIOCHEMISTRY (TWO-WEEK STUDY : SUMMARY)

MOUSE: FEMALE

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	TOTAL PROTEIN g／dℓ	ALBUMIN g／dℓ	A/G RATIO	T-BILIRUBIN mg／dℓ	GLUCOSE mg／dℓ	T-CHOLESTEROL mg／dℓ	GOT I U／ℓ
Control	5	5.2± 0.2	3.1± 0.1	1.5± 0.0	0.29± 0.06	270± 20	76± 5	42± 2
1778ppm	5	5.0± 0.1	3.0± 0.2	1.5± 0.1	0.29± 0.12	274± 35	60± 3**	44± 7
2667ppm	5	5.0± 0.1	3.1± 0.1	1.6± 0.1	0.33± 0.09	272± 25	62± 10*	36± 5
4000ppm	5	5.1± 0.1	3.1± 0.0	1.6± 0.1	0.35± 0.12	264± 24	65± 5	41± 8
6000ppm	5	5.1± 0.2	3.0± 0.1	1.5± 0.1	0.34± 0.12	264± 17	69± 10	41± 4
9000ppm	5	5.2± 0.2	3.1± 0.1	1.5± 0.1	0.30± 0.15	264± 27	70± 5	57± 33

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	GPT IU/ℓ		LDH IU/ℓ		CPK IU/ℓ		UREA NITROGEN mg/dℓ		SODIUM mEq/ℓ		POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ	
Control	5	12±	4	253±	83	69±	36	23.0±	3.5	151±	2	4.7±	0.6	118±	3
1778ppm	5	14±	3	226±	23	66±	44	24.4±	2.2	149±	2	4.5±	0.2	118±	3
2667ppm	5	11±	2	197±	28	42±	20	26.6±	2.4	150±	2	4.5±	0.3	118±	2
4000ppm	5	11±	3	234±	96	39±	12	27.9±	7.5	149±	1	4.8±	0.1	119±	1
6000ppm	5	11±	1	236±	30	53±	27	29.5±	4.3	153±	3	4.6±	0.2	118±	1
9000ppm	5	16±	10	316±	113	106±	109	36.6±	7.0**	156±	5*	5.4±	0.3*	116±	3

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	CALCIUM mg/dl	INORGANIC PHOSPHORUS mg/dl
Control	5	9.0± 0.4	7.9± 1.2
1778ppm	5	8.9± 0.3	8.2± 0.6
2667ppm	5	9.0± 0.4	7.8± 1.2
4000ppm	5	9.0± 0.3	7.5± 1.4
6000ppm	5	9.1± 0.2	8.3± 1.0
9000ppm	5	9.0± 0.3	8.8± 1.7

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 8-1

ORGAN WEIGHT (TWO-WEEK STUDY : SUMMARY),ABSOLUTE

RAT : MALE

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	173± 7	0.378± 0.029	0.042± 0.009	1.997± 0.143	0.622± 0.039	0.767± 0.023
1778ppm	5	172± 3	0.384± 0.027	0.038± 0.004	2.085± 0.149	0.601± 0.038	0.780± 0.038
2667ppm	5	166± 6	0.364± 0.027	0.040± 0.005	2.076± 0.151	0.574± 0.038	0.756± 0.047
4000ppm	5	147± 11	0.313± 0.011	0.043± 0.010	1.833± 0.258	0.533± 0.044*	0.722± 0.039
6000ppm	5	119± 19*	0.191± 0.079*	0.037± 0.005	1.498± 0.514*	0.432± 0.054**	0.614± 0.047**
9000ppm	5	85± 13**	0.057± 0.029**	0.034± 0.003	0.908± 0.211**	0.349± 0.040**	0.557± 0.014**

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	1.364± 0.052	0.391± 0.026	6.672± 0.554	1.696± 0.029
1778ppm	5	1.380± 0.044	0.398± 0.030	6.699± 0.251	1.697± 0.047
2667ppm	5	1.327± 0.048	0.392± 0.020	6.491± 0.519	1.703± 0.073
4000ppm	5	1.224± 0.069	0.336± 0.039	5.478± 0.649*	1.675± 0.052
6000ppm	5	1.101± 0.181*	0.266± 0.051**	4.280± 0.976**	1.627± 0.058
9000ppm	5	0.890± 0.084**	0.165± 0.053**	2.645± 0.477**	1.587± 0.052*

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 8-2

ORGAN WEIGHT (TWO-WEEK STUDY : SUMMARY),ABSOLUTE

RAT : FEMALE

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	130± 5	0.306± 0.013	0.046± 0.006	0.073± 0.016	0.470± 0.023	0.660± 0.017
1778ppm	5	126± 4	0.323± 0.017	0.044± 0.003	0.073± 0.017	0.508± 0.027	0.614± 0.023
2667ppm	5	119± 8	0.286± 0.019	0.043± 0.007	0.064± 0.019	0.456± 0.036	0.617± 0.032
4000ppm	5	114± 4**	0.279± 0.036	0.044± 0.004	0.062± 0.006	0.432± 0.022	0.623± 0.032
6000ppm	5	103± 11**	0.193± 0.093*	0.042± 0.008	0.059± 0.011	0.372± 0.041**	0.565± 0.048**
9000ppm	1	68± 0 ?	0.034± 0.000 ?	0.039± 0.000 ?	0.042± 0.000 ?	0.332± 0.000 ?	0.557± 0.000 ?

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	1.046± 0.034	0.326± 0.019	4.437± 0.389	1.625± 0.046
1778ppm	5	1.055± 0.016	0.298± 0.014	4.458± 0.254	1.597± 0.058
2667ppm	5	1.035± 0.071	0.288± 0.024	4.080± 0.404	1.583± 0.049
4000ppm	5	1.048± 0.015	0.277± 0.012*	3.930± 0.103	1.564± 0.033
6000ppm	5	0.951± 0.115	0.241± 0.048**	3.549± 0.382**	1.566± 0.044
9000ppm	1	0.853± 0.000 ?	0.135± 0.000 ?	2.717± 0.000 ?	1.499± 0.000 ?

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX A 8-3

ORGAN WEIGHT (TWO-WEEK STUDY : SUMMARY),ABSOLUTE

MOUSE: MALE

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	24.0± 1.3	0.049± 0.008	0.012± 0.002	0.182± 0.014	0.124± 0.010	0.151± 0.021
1778ppm	5	24.9± 0.5	0.054± 0.009	0.014± 0.004	0.153± 0.022	0.130± 0.008	0.153± 0.013
2667ppm	5	23.8± 1.8	0.047± 0.010	0.013± 0.003	0.176± 0.031	0.126± 0.009	0.141± 0.016
4000ppm	5	24.8± 1.1	0.054± 0.005	0.013± 0.001	0.179± 0.026	0.130± 0.011	0.154± 0.008
6000ppm	5	23.5± 1.0	0.047± 0.008	0.014± 0.001	0.167± 0.016	0.127± 0.008	0.147± 0.012
9000ppm	5	21.0± 3.8	0.035± 0.017	0.012± 0.003	0.183± 0.019	0.114± 0.021	0.144± 0.015

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.428± 0.181	0.063± 0.025	1.197± 0.132	0.446± 0.012
1778ppm	5	0.381± 0.017	0.057± 0.007	1.216± 0.073	0.431± 0.014
2667ppm	5	0.445± 0.123	0.056± 0.007	1.142± 0.208	0.445± 0.009
4000ppm	5	0.404± 0.018	0.055± 0.006	1.235± 0.086	0.445± 0.010
6000ppm	5	0.392± 0.039	0.052± 0.007	1.110± 0.070	0.433± 0.016
9000ppm	5	0.364± 0.024	0.042± 0.016	0.984± 0.280	0.432± 0.019

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 8-4

ORGAN WEIGHT (TWO-WEEK STUDY : SUMMARY),ABSOLUTE

MOUSE: FEMALE

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	19.5± 0.4	0.072± 0.006	0.015± 0.001	0.026± 0.008	0.113± 0.007	0.142± 0.011
1778ppm	5	19.3± 1.1	0.067± 0.009	0.015± 0.001	0.025± 0.004	0.107± 0.009	0.142± 0.008
2667ppm	5	19.0± 0.9	0.070± 0.008	0.013± 0.001	0.025± 0.005	0.105± 0.006	0.133± 0.005
4000ppm	5	19.3± 1.1	0.069± 0.007	0.012± 0.003	0.027± 0.006	0.110± 0.007	0.140± 0.006
6000ppm	5	18.8± 0.8	0.064± 0.006	0.012± 0.003	0.027± 0.006	0.101± 0.008	0.134± 0.006
9000ppm	5	18.6± 0.6	0.062± 0.006	0.013± 0.003	0.026± 0.004	0.100± 0.008	0.135± 0.011

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.272± 0.005	0.062± 0.009	0.923± 0.044	0.459± 0.012
1778ppm	5	0.276± 0.020	0.058± 0.003	0.901± 0.085	0.441± 0.007
2667ppm	5	0.279± 0.009	0.058± 0.007	0.913± 0.055	0.444± 0.023
4000ppm	5	0.288± 0.015	0.060± 0.005	0.911± 0.086	0.444± 0.009
6000ppm	5	0.287± 0.018	0.058± 0.006	0.847± 0.062	0.438± 0.007
9000ppm	5	0.289± 0.013	0.059± 0.006	0.846± 0.026	0.430± 0.009**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 9-1

ORGAN WEIGHT (TWO-WEEK STUDY : SUMMARY),RELATIVE

RAT : MALE

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	173± 7	0.218± 0.024	0.024± 0.005	1.152± 0.072	0.359± 0.014	0.443± 0.019
1778ppm	5	172± 3	0.224± 0.015	0.022± 0.002	1.213± 0.069	0.350± 0.022	0.454± 0.021
2667ppm	5	166± 6	0.219± 0.012	0.024± 0.003	1.251± 0.077	0.346± 0.021	0.455± 0.019
4000ppm	5	147± 11	0.213± 0.016	0.030± 0.008	1.240± 0.108	0.362± 0.018	0.492± 0.032
6000ppm	5	119± 19*	0.154± 0.050**	0.032± 0.002	1.231± 0.296	0.365± 0.022	0.524± 0.076
9000ppm	5	85± 13**	0.063± 0.023**	0.040± 0.005*	1.061± 0.140	0.412± 0.043*	0.662± 0.088**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.787± 0.013	0.225± 0.014	3.843± 0.168	0.979± 0.036
1778ppm	5	0.803± 0.029	0.232± 0.018	3.901± 0.179	0.988± 0.040
2667ppm	5	0.800± 0.032	0.237± 0.021	3.807± 0.222	1.026± 0.024
4000ppm	5	0.831± 0.035	0.228± 0.013	3.710± 0.215	1.140± 0.059
6000ppm	5	0.924± 0.062**	0.222± 0.018	3.561± 0.361	1.389± 0.191*
9000ppm	5	1.050± 0.072**	0.189± 0.035	3.088± 0.092**	1.884± 0.220**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 9-2

ORGAN WEIGHT (TWO-WEEK STUDY : SUMMARY),RELATIVE

RAT : FEMALE

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	130± 5	0.236± 0.007	0.036± 0.004	0.056± 0.014	0.363± 0.015	0.510± 0.022
1778ppm	5	126± 4	0.257± 0.013	0.035± 0.004	0.058± 0.015	0.404± 0.018**	0.489± 0.015
2667ppm	5	119± 8	0.241± 0.008	0.036± 0.004	0.054± 0.013	0.384± 0.017	0.520± 0.013
4000ppm	5	114± 4**	0.244± 0.026	0.039± 0.004	0.054± 0.006	0.378± 0.013	0.546± 0.034
6000ppm	5	103± 11**	0.182± 0.081	0.041± 0.004	0.057± 0.006	0.361± 0.022	0.549± 0.038
9000ppm	1	68± 0 ?	0.050± 0.000 ?	0.057± 0.000 ?	0.062± 0.000 ?	0.488± 0.000 ?	0.819± 0.000 ?

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.808± 0.021	0.252± 0.015	3.419± 0.199	1.255± 0.048
1778ppm	5	0.841± 0.024	0.238± 0.010	3.551± 0.208	1.273± 0.072
2667ppm	5	0.872± 0.020**	0.242± 0.007	3.428± 0.123	1.335± 0.060
4000ppm	5	0.919± 0.025**	0.242± 0.013	3.443± 0.083	1.372± 0.063
6000ppm	5	0.921± 0.021**	0.231± 0.028	3.439± 0.095	1.528± 0.135**
9000ppm	1	1.254± 0.000 ?	0.199± 0.000 ?	3.996± 0.000 ?	2.204± 0.000 ?

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX A 9-3

ORGAN WEIGHT (TWO-WEEK STUDY : SUMMARY),RELATIVE

MOUSE: MALE

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	24.0± 1.3	0.205± 0.033	0.051± 0.008	0.758± 0.082	0.516± 0.052	0.628± 0.067
1778ppm	5	24.9± 0.5	0.216± 0.034	0.054± 0.014	0.614± 0.082	0.522± 0.029	0.615± 0.060
2667ppm	5	23.8± 1.8	0.198± 0.035	0.056± 0.011	0.747± 0.167	0.532± 0.019	0.600± 0.104
4000ppm	5	24.8± 1.1	0.218± 0.015	0.054± 0.006	0.721± 0.084	0.525± 0.028	0.620± 0.029
6000ppm	5	23.5± 1.0	0.198± 0.027	0.061± 0.006	0.710± 0.043	0.541± 0.037	0.622± 0.036
9000ppm	5	21.0± 3.8	0.157± 0.066	0.059± 0.010	0.885± 0.103	0.542± 0.030	0.697± 0.081

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	1.796± 0.825	0.266± 0.112	4.988± 0.558	1.857± 0.083
1778ppm	5	1.532± 0.097	0.227± 0.028	4.878± 0.270	1.730± 0.035
2667ppm	5	1.902± 0.667	0.239± 0.041	4.773± 0.595	1.877± 0.135
4000ppm	5	1.627± 0.050	0.223± 0.017	4.978± 0.312	1.794± 0.051
6000ppm	5	1.662± 0.098	0.220± 0.022	4.717± 0.216	1.839± 0.071
9000ppm	5	1.769± 0.266	0.191± 0.057	4.586± 0.660	2.110± 0.398

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 9-4

ORGAN WEIGHT (TWO-WEEK STUDY : SUMMARY),RELATIVE

MOUSE: FEMALE

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	19.5± 0.4	0.367± 0.037	0.078± 0.006	0.133± 0.041	0.580± 0.040	0.729± 0.056
1778ppm	5	19.3± 1.1	0.348± 0.050	0.079± 0.008	0.131± 0.016	0.552± 0.042	0.734± 0.042
2667ppm	5	19.0± 0.9	0.369± 0.027	0.067± 0.007	0.133± 0.023	0.552± 0.035	0.697± 0.033
4000ppm	5	19.3± 1.1	0.357± 0.032	0.064± 0.012	0.140± 0.030	0.568± 0.024	0.727± 0.040
6000ppm	5	18.8± 0.8	0.339± 0.021	0.066± 0.013	0.141± 0.024	0.539± 0.041	0.714± 0.054
9000ppm	5	18.6± 0.6	0.336± 0.039	0.068± 0.016	0.142± 0.024	0.540± 0.036	0.727± 0.039

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	1.390± 0.044	0.317± 0.048	4.727± 0.271	2.352± 0.077
1778ppm	5	1.425± 0.056	0.303± 0.020	4.656± 0.306	2.288± 0.161
2667ppm	5	1.467± 0.063	0.306± 0.036	4.798± 0.198	2.338± 0.208
4000ppm	5	1.491± 0.046*	0.311± 0.021	4.713± 0.302	2.304± 0.077
6000ppm	5	1.522± 0.084**	0.305± 0.021	4.494± 0.257	2.327± 0.074
9000ppm	5	1.555± 0.041**	0.316± 0.021	4.560± 0.176	2.316± 0.045

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 10-1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

RAT : MALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 0 1 (%)	Control 0 2 (%)	Control 0 3 (%)	Control 0 4 (%)	1778ppm 0 1 (%)	1778ppm 0 2 (%)	1778ppm 0 3 (%)	1778ppm 0 4 (%)	2667ppm 0 1 (%)	2667ppm 0 2 (%)	2667ppm 0 3 (%)	2667ppm 0 4 (%)	4000ppm 0 1 (%)	4000ppm 0 2 (%)	4000ppm 0 3 (%)	4000ppm 0 4 (%)
[Hematopoietic system]																		
bone marrow		< 0>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	congestion	(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	decreased hematopoiesis	(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
thymus		< 0>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	atrophy	(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	karyorrhexis	(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
spleen		< 0>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	atrophy	(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Urinary system]																		
kidney		< 0>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	vacuolic change:straight portion of proximal tubule	(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Endocrine system]																		
adrenal		< 0>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	hemorrhage	(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

Grade 1 : Slight 2 : Moderate 3 : Ma rked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : a / b * 100

Organ	Findings	Group Name	6000ppm				9000ppm			
		No. of Animals on Study	0				2			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]										
bone marrow			< 0>				< 2>			
	congestion		- (-)	- (-)	- (-)	- (-)	0 (0)	2 (100)	0 (0)	0 (0)
	decreased hematopoiesis		- (-)	- (-)	- (-)	- (-)	1 (50)	1 (50)	0 (0)	0 (0)
thymus			< 0>				< 2>			
	atrophy		- (-)	- (-)	- (-)	- (-)	0 (0)	0 (0)	2 (100)	0 (0)
	karyorrhexis		- (-)	- (-)	- (-)	- (-)	2 (100)	0 (0)	0 (0)	0 (0)
spleen			< 0>				< 2>			
	atrophy		- (-)	- (-)	- (-)	- (-)	0 (0)	1 (50)	0 (0)	0 (0)
[Urinary system]										
kidney			< 0>				< 2>			
	vacuolic change:straight portion of proximal tubule		- (-)	- (-)	- (-)	- (-)	1 (50)	1 (50)	0 (0)	0 (0)
[Endocrine system]										
adrenal			< 0>				< 2>			
	hemorrhage		- (-)	- (-)	- (-)	- (-)	1 (50)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Ma rked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : a / b * 100

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 0 1 (%)	Control 0 2 (%)	Control 0 3 (%)	Control 0 4 (%)	1778ppm 0 1 (%)	1778ppm 0 2 (%)	1778ppm 0 3 (%)	1778ppm 0 4 (%)	2667ppm 0 1 (%)	2667ppm 0 2 (%)	2667ppm 0 3 (%)	2667ppm 0 4 (%)	4000ppm 0 1 (%)	4000ppm 0 2 (%)	4000ppm 0 3 (%)	4000ppm 0 4 (%)
[Reproductive system]																		
testis			< 0>				< 0>				< 0>				< 0>			
	atrophy		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
epididymis			< 0>				< 0>				< 0>				< 0>			
	debris of spermatic elements		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)

Grade 1 : Slight 2 : Moderate 3 : Ma rked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : a / b * 100

Organ	Findings	Group Name	6000ppm				9000ppm			
		No. of Animals on Study	0				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]										
testis			< 0>				< 2>			
	atrophy		-	-	-	-	1	1	0	0
			(-)	(-)	(-)	(-)	(50)	(50)	(0)	(0)
epididymis			< 0>				< 2>			
	debris of spermatic elements		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(50)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Ma rked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : a / b * 100

APPENDIX A 10-2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

RAT : FEMALE : DEAD AND MORIBUND ANIMALS

Organ	Findings	Group Name	Control				1778ppm				2667ppm				4000ppm			
		No. of Animals on Study	0				0				0				0			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
bone marrow			< 0>				< 0>				< 0>				< 0>			
	congestion		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	decreased hematopoiesis		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
thymus			< 0>				< 0>				< 0>				< 0>			
	atrophy		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	karyorrhexis		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
spleen			< 0>				< 0>				< 0>				< 0>			
	atrophy		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	karyorrhexis		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
[Urinary system]																		
kidney			< 0>				< 0>				< 0>				< 0>			
	mineralization:cortico-medullary junction		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)

Grade 1 : Slight 2 : Moderate 3 : Ma rked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : a / b * 100

Organ	Findings	Group Name	6000ppm				9000ppm			
		No. of Animals on Study	1				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
bone marrow			< 1>				< 2>			
	congestion		0	1	0	0	0	2	0	0
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
	decreased hematopoiesis		0	1	0	0	0	2	0	0
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
thymus			< 1>				< 2>			
	atrophy		0	0	1	0	0	0	2	0
			(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)
	karyorrhexis		0	0	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
spleen			< 1>				< 2>			
	atrophy		0	1	0	0	2	0	0	0
			(0)	(100)	(0)	(0)	(100)	(0)	(0)	(0)
	karyorrhexis		0	0	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
[Urinary system]										
kidney			< 1>				< 2>			
	mineralization:cortico-medullary junction		0	0	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Ma rked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : a / b * 100

Organ	Findings	Group Name	Control				1778ppm				2667ppm				4000ppm			
		No. of Animals on Study	0				0				0				0			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
adrenal			< 0>				< 0>				< 0>				< 0>			
	hemorrhage		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

Grade 1 : Slight 2 : Moderate 3 : Ma rked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : a / b * 100

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name	6000ppm				9000ppm			
		No. of Animals on Study	1				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]										
adrenal			< 1>				< 2>			
	hemorrhage		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Ma rked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : a / b * 100

APPENDIX A 10-3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

RAT : MALE : SACRIFICED ANIMALS

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 1	Control 2	Control 3	Control 4	1778ppm 1	1778ppm 2	1778ppm 3	1778ppm 4	2667ppm 1	2667ppm 2	2667ppm 3	2667ppm 4	4000ppm 1	4000ppm 2	4000ppm 3	4000ppm 4
			2				2				2				2			
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
bone marrow		< a >	< 2>				< 2>				< 2>				< 2>			
	congestion	b	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(c)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	decreased hematopoiesis	b	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(c)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thymus		< a >	< 2>				< 2>				< 2>				< 2>			
	atrophy	b	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(c)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	karyorrhexis	b	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(c)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen		< a >	< 2>				< 2>				< 2>				< 2>			
	karyorrhexis	b	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(c)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Reproductive system]																		
testis		< a >	< 2>				< 2>				< 2>				< 2>			
	atrophy	b	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(c)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
epididymis		< a >	< 2>				< 2>				< 2>				< 2>			
	debris of spermatic elements	b	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(c)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Ma rked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : a / b * 100

Organ	Findings	Group Name	6000ppm				9000ppm			
		No. of Animals on Study	2				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
bone marrow			< 2>				< 2>			
	congestion		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)
	decreased hematopoiesis		0	0	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
thymus			< 2>				< 2>			
	atrophy		0	0	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)
	karyorrhexis		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
spleen			< 2>				< 2>			
	karyorrhexis		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
[Reproductive system]										
testis			< 2>				< 2>			
	atrophy		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)
epididymis			< 2>				< 2>			
	debris of spermatic elements		0	0	0	0	1	1	0	0
			(0)	(0)	(0)	(0)	(50)	(50)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Ma rked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : a / b * 100

APPENDIX A 10-4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

RAT : FEMALE : SACRIFICED ANIMALS

STUDY NO. : 0222
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name	Control				1778ppm				2667ppm				4000ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasal cavit			< 2>				< 2>				< 2>				< 2>			
	respiratory metaplasia:gland		1 (50)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]																		
bone marrow			< 2>				< 2>				< 2>				< 2>			
	decreased hematopoiesis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
thymus			< 2>				< 2>				< 2>				< 2>			
	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	karyorrhexis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Digestive system]																		
liver			< 2>				< 2>				< 2>				< 2>			
	hemorrhage		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Urinary system]																		
kidney			< 2>				< 2>				< 2>				< 2>			
	basophilic change		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Ma rked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : a / b * 100

Organ	Findings	Group Name	6000ppm				9000ppm			
		No. of Animals on Study	2				1			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			< 2>				< 1>			
	respiratory metaplasia:gland		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]										
bone marrow			< 2>				< 1>			
	decreased hematopoiesis		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
thymus			< 2>				< 1>			
	atrophy		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
	karyorrhexis		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
[Digestive system]										
liver			< 2>				< 1>			
	hemorrhage		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
[Urinary system]										
kidney			< 2>				< 1>			
	basophilic change		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Ma rked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : a / b * 100

Organ	Findings	Group Name	Control				1778ppm				2667ppm				4000ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
[Urinary system]																		
kidney																		
	mineralization:cortico-medullary junction		< 2>				< 2>				< 2>				< 2>			
			0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Ma rked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : a / b * 100

Organ	Findings	Group Name	6000ppm				9000ppm			
		No. of Animals on Study	2				1			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]										
kidney										
	mineralization:cortico-medullary junction		< 2>				< 1>			
			0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Ma rked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : a / b * 100

APPENDIX A 10-5

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

MOUSE: MALE : SACRIFICED ANIMALS

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0- 2W)

Organ	Findings	Group Name	Control				1778ppm				2667ppm				4000ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
liver			< 2>				< 2>				< 2>				< 2>			
	granulation		2	0	0	0	0	1	0	0	1	1	0	0	1	0	0	0
			(100)	(0)	(0)	(0)	(0)	(50)	(0)	(0)	(50)	(50)	(0)	(0)	(50)	(0)	(0)	(0)
[Urinary system]																		
kidney			< 2>				< 2>				< 2>				< 2>			
	basophilic change		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hydronephrosis		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Ma rked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : a / b * 100

Organ	Findings	Group Name	6000ppm				9000ppm			
		No. of Animals on Study	2				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]										
liver			< 2>				< 2>			
	granulation		1	1	0	0	0	0	0	0
			(50)	(50)	(0)	(0)	(0)	(0)	(0)	(0)
[Urinary system]										
kidney			< 2>				< 2>			
	basophilic change		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hydronephrosis		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Ma rked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : a / b * 100

APPENDIX A 10-6

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

MOUSE: FEMALE : SACRIFICED ANIMALS

STUDY NO. : 0223
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0- 2W)

Organ	Findings	Group Name	Control				1778ppm				2667ppm				4000ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
liver			< 2>				< 2>				< 2>				< 2>			
	inflammation		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
	granulation		1	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(50)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Ma rked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : a / b * 100

Organ	Findings	Group Name	6000ppm				9000ppm			
		No. of Animals on Study	2				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]										
liver										
	inflammation		< 2>				< 2>			
			0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Ma rked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : a / b * 100

APPENDIX A 11-1

IDENTITY OF GLYOXAL

(TWO-WEEK STUDIES)

IDENTITY OF GLYOXAL(TWO-WEEK STUDIES)

Test Substance Lot No.: WDL5585

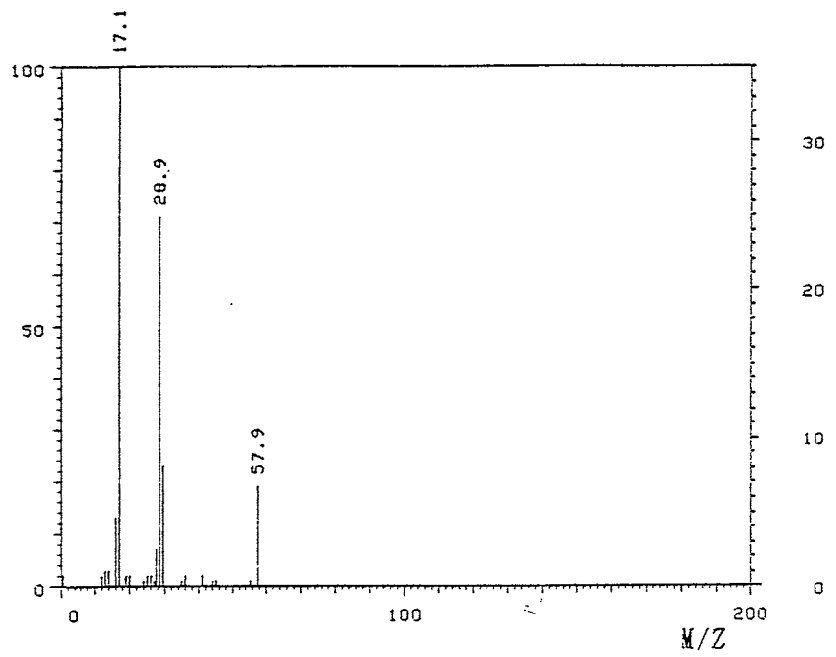
1. Spectral data

Mass Spectrometry

Instrument: Hitachi M-80B Mass Spectrometer

Ionization: EI(Electron Ionization)

Ionization Voltage: 70eV



Mass Spectrum of Test Substance

Results:	Determined Molecular and Fragment Peak(M/Z)	Literature Value* Molecular and Fragment Peak(M/Z)
	57.9	58.0
	28.9	29.0
	17.1	17.0
		(*EPA/NIH Mass Spectral Data Base (1978) V. 1, p. 7.)

2. Conclusions: The result of the mass spectrum agreed with the literature value. Consequently, the test substance was identified as glyoxal.

APPENDIX A 11-2

STABILITY OF GLYOXAL

(TWO-WEEK STUDIES)

STABILITY OF GLYOXAL(TWO-WEEK STUDIES)

Test Substance Lot No.: WDL5585

1. Sample storage: This lot was used from 1992.10.26 to 1992.11.16. Test substance was stored at room temperature.

2. Gas Chromatography

Instrument: Hewlett Packard 5890A Gass Chromatograph

Column: Methyl Silicone(0.2mmϕ × 50m)

Column Temperature: 200°C

Flow Rate: 1 ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1 μl

Pre-Treatment: Glyoxal was allowed to react with quinoxaline, and analyzed. First, 50% hydroxylammonium chloride(0.02ml), 36% hydrochloric acid(0.1ml), 4% o-phenylene diamine dihydrochloride(0.05ml) were added to a glyoxal solution (1ml). This mixture was stirred at 75°C for 0.5 hr. Then, this solution was extracted with ethyl acetate(2ml) and analyzed.

Results: Chromatogram indicated one major peak(peak No.2) and solvent peak(peak No.1) analyzed at 1992.10.9 and one major peak(peak No.2) and solvent peak(peak No.1) analyzed at 1992.11.17. The new treace impurity peak in the test substance analyzed at 1992.11.17 was not detected.

Date	Peak No.	Retention Time(min)	Retention Time Relative to Major Peak	Area (percent of Major peak)
1992.10.9	1	2.838(Solvent peak)		
(date analyzed)	2	3.473	1.00	100
1992.11.17	1	2.837(Solvent peak)		
(date analyzed)	2	3.47	1.00	100

3. Conclusions: The results indicated that the test sabstance did not change when stored in the dark at 5°C during this period(for about 6 weeks).

APPENDIX A 11-3

CONCENTRATION GLYOXAL IN DRINKING WATER

(TWO-WEEK STUDIES)

CONCENTRATION OF GLYOXAL IN DRINKING WATER(TWO-WEEK STUDIES)

(Rat)(Mouse)

	Target Concentration(ppm)				
Date analyzed	1778	2667	4000	6000	9000
1992.10.26	1702.9(95.8)*	2644.7(99.2)	3972.5(99.3)	5893.9(98.2)	8940.6(99.3)

(*) % of target concentration

Analytical method : The sample were analyzed by the gas chromatography.

Instrument : Hewlett Packard 5890A
Column : METHYL SILICONE(0.2mmϕ × 50m)
Column Temperature: 200℃
Carrier : He
Flow Rate : 1ml/min
Detector : FID(Flame Ionization Detector)
Injection Volume : 1μl

Pre-Treatment : Glyoxal was allowed to react with quinoxaline, and analyzed. First, 50% hydroxylammonium chloride(0.02ml), 36% hydrochloric acid(0.1ml), 4% o-phenylene diamine dihydrochloride(0.05ml) were added to a glyoxal solution(1ml). This mixture was stirred at 75℃ for 0.5 hr. Then, this solution was extracted with ethyl acetate(2ml) and analyzed.

APPENDIX A 11-4

STABILITY OF GLYOXAL IN DRINKING WATER

(TWO-WEEK STUDIES)

STABILITY OF GLYOXAL IN DRINKING WATER(TWO-WEEK STUDIES)

(Rat)

Date analyzed	Target Concentration(ppm)	
	1778	9000
1992.10.09(a)	1825	9148
1992.10.16(b)	1799	8730

(MOUSE)

Date analyzed	Target Concentration(ppm)	
	1778	9000
1992.10.09(a)	1825	9148
1992.10.16(b)	1872	9085

(a) Date of preparation
(b) The stability of glyoxal in drinking water was established for 7 days when stored at 25℃.

Analytical method: The sample were analyzed by the gas chromatography.

Instrument : Hewlett Packard 5890A
Column : METHYL SILICONE(0.2mmϕ × 50m)
Column Temperature: 200℃
Carrier : He
Flow Rate : 1ml/min
Detector : FID(Flame Ionization Detector)
Injection Volume : 1μl

Pre-Treatment : Glyoxal was allowed to react with quinoxaline, and analyzed. First, 50% hydroxylammonium chloride(0.02ml), 36% hydrochloric acid(0.1ml), 4% o-phenylene diamine dihydrochloride(0.05ml) were added to a glyoxal solution(1ml). This mixture was stirred at 75℃ for 0.5 hr. Then, this solution was extracted with ethyl acetate(2ml) and analyzed.